REMARKS

Claims 1, 2, 11, 13-18, 20, 21, and 23-29 constitute the pending claims in the present application. Claims 1, 2, 11, 13-18, 20, 21, and 23-29 have been amended. Applicants assert that no new matter has been introduced in the amendments. Claims 3-10, 12, 19, 22, and 30 have been cancelled without prejudice to prosecution. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Objection to the drawings. The drawings are objected to because they are difficult to read. Applicants enclose herewith replacement drawings for figures 1 to 3 as requested by the Examiner. Reconsideration and withdrawal of this objection is respectfully requested.

Objection to the specification. The specification is objected to because the reference to and brief description of the drawings are inadequate. Applicants have amended the specification as requested. Applicants respectfully request reconsideration and withdrawal of this objection.

Rejection based on 35 U.S.C. 112, first paragraph, written description. Claims 1, 2, 11, 13-18, 20, 21, and 23-29 are rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants traverse this rejection to the extent it is maintained over the claims as amended.

The Office Action states that the terms "prodrug or metabolic derivative thereof" and "as valence and stability permit" have insufficient basis in the specification (Office Action at page 3-4). Applicants have removed these terms from the claims, thereby rendering this rejection moot. Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection based on 35 U.S.C. 112, first paragraph, enablement. Claims 1, 2, 11, 13-18, 20, 21, and 23-29 are rejected under 35 U.S.C. 112, first paragraph. Applicants traverse this rejection to the extent it is maintained over the claims as amended.

The Office Action states that "the specification, while being enabling for a method for **reducing** hearing impairment caused by the platinum-containing antineoplastic agent, cisplatin, by administration of 2-thiouracil prior to the cisplatin exposure, does not reasonably provide enablement for **preventing** hearing impairment caused by the platinum-containing antineoplastic agent, cisplatin, or **preventing or reducing** hearing impairment caused by other chemical agents (*i.e.*, aminoglycoside antibiotics, ototoxic diuretics, or certain quinine-like compounds), noise or aging." (Office Action at page 5, emphases in the original)

Applicants disagree and respectfully direct the Examiner's attention to page 5, lines 8-10 which define the term "preventing" as "reduc[ing] the risk of occurrence of an abnormal biological or a medical event, such as hearing loss, in a cell, a tissue, a system, animal or human." Applicants further direct the Examiner's attention to Example 1 on page 32, wherein animals were first injected with test compounds and then subsequently treated with cisplatin. Applicants assert that such treatment with test compounds was a preventative measure to avoid hearing loss caused by ototoxic compounds, such as cisplatin, and that the results of these experiments correlate exactly with the term "prevent" as it is defined in the specification. The Examiner has offered neither evidence nor argument to refute Applicants' evidence, but instead appears to be relying on some other definition of the word "prevent". Pursuant to MPEP 2106, "[w]here an explicit definition is provided by the applicant for a term, that definition will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) (meaning of words used in a claim is not construed in a 'lexicographic vacuum, but in the context of the specification and drawings')." Applicants therefore assert that the prevention of hearing impairment as defined in the specification is enabled. Applicants respectfully request reconsideration and withdrawal of this rejection.

The Office Action states that "the specification does not provide guidance or a working example for... **reducing** hearing impairment caused by other chemical agents (*i.e.*, aminoglycoside antibiotics, ototoxic diuretics, or certain quinine-like compounds), noise or aging." (Office Action at page 8-9, emphasis in the original)

Applicants disagree and respectfully direct the Examiner's attention to page 2, lines 24-28 of the specification which states that "[w]hile the efficacy of 2-thio-nitrogen-containing compounds disclosed herein may be due to their antioxidative properties *vis-à-vis* reactive oxygen species generated by, for instance, an aminoglycoside antibiotic or a platinum-containing antineoplastic agent, the efficacy may also be due to another mechanism, such as inhibition of nitric oxide synthetase by the otoprotective compounds disclosed in the present invention." Accordingly, Applicants assert that by providing guidance and working examples for the reduction or treatment of hearing loss caused by cisplatin, Applicants have sufficiently enabled the treatment or reduction of hearing loss caused by anything that invokes this same destructive mechanism. Additionally, pursuant to MPEP 2164.04, "[i]n order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).... A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.... *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971)." Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection based on 35 U.S.C. 102(e). Claims 1, 11, 13, 15, 17, 21, and 29 are rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Laurell (2003/0180388). Applicants traverse this rejection to the extent it is maintained over the claims as amended.

The Office Action states that Laurell "teach[es] the administration of thiourea or dimethylthiourea to reduce chemical induced hearing loss." (Office Action at page 11) The claims as amended do not include thiourea or dimethylthiourea within the scope of the claims; therefore, Laurell does not teach or suggest all of the elements of the claims as amended. Accordingly, Laurell cannot anticipate claims 1, 11, 13, 15, 17, 21, or 29. Applicants respectfully request reconsideration and withdrawal of this rejection.

Rejection based on 35 U.S.C. 102(b). Claims 21, and 23-28 are rejected under 35 U.S.C. 102(b) as being allegedly anticipated by Principles of Pharmacology. Applicants traverse this rejection to the extent it is maintained over the claims as amended.

The Office Action alleges that Principles of Pharmacology teaches the compositions and dosage forms of thiourylenes, including methimazole (MMI), propylthiouracil (PTU), and carbimazole to inhibit thyroid hormone synthesis.

Applicants assert that the claims as amended do not include the thiourylenes disclosed in Principles of Pharmacology, therefore Principles of Pharmacology does not teach or suggest all of the elements of the claims. Accordingly, the reference cannot anticipate claims 21 and 23-28. Applicants respectfully request reconsideration and withdrawal of this rejection.

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. Applicants believe no additional fee is due with this response, aside from the fee for the Petition for Extension of Time. However, if a fee is due, please charge our Deposit Account No. 18-1945, under Order No. SEPR-P01-056 from which the undersigned is authorized to draw.

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Respectfully submitted,

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